REMARKS

Applicants have amended their claims herein to better clarify the invention. Claim 1 recites an oral dosage form comprising a bi-layer tablet and an encapsulant wherein the oral dosage form is formed to include an aperture extending through the encapsulant and into the first layer. Support can be found in the Specification on Page 8 at Lines 19-24, in FIG. 3 at elements 310, 312, and 314.

No new matter has been entered. Reexamination and reconsideration of the application, as amended, is respectfully requested.

Claims 1-6, stand rejected under 35 USC 103(a) as being unpatentable over Mayer et al (U.S. Pat. No. 5,869,498) in view of Guittard et al. (U.S. Pat. No. 6,124,355).

Mayer et al. teach a dosage form comprising a pharmacologically effective amount of a first component, a pharmacologically effective amount of a second component, and an analgesia-enhancing amount of a third component. Col. 2 / Lines 30-48. Mayer et al. teach two formulations comprising oxycodone.

In Example 10, Mayer et al. teach a dosage form comprising a oxycodone hydrochloride, acetaminophen, and dextromethorphan hydrobromide, wherein the weight ratio between the oxycodone hydrochloride and the dextromethorphan hydrobromide is 1:6.

In Example 11, Mayer et al. teach a dosage form comprising a oxycodone hydrochloride/oxycodone terephthalate, aspirin, and dextromethorphan hydrobromide, wherein the weight ratio between the oxycodone elements and the dextromethorphan hydrobromide is 1:615.

Mayer et al. teach away from Applicants' claim 1, as amended herein. "A reference

CHANDLER & UDALL, LLP
4801 E. BROADWAY BLVD
Tucson, Arizona 85711

TEL 520-741-7636
FAX 520-746-9114

may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994); *see KSR*, 127 S. Ct. at 1739-40 (explaining that when the prior art teaches away from a combination, that combination is more likely to be nonobvious).

One of ordinary skill in the art following the teachings of Mayer et al. would find motivation to formulation a dosage form wherein the weight ratio between the oxycodone hydrochloride and the dextromethorphan hydrobromide is 1:6 or greater. On the other hand, one of ordinary skill in the art would find no motivation to formulate a dosage form wherein the weight ratio between the oxycodone hydrochloride and the dextromethorphan hydrobromide is 1:5, as recited by Applicants' claim 1, as amended herein.

The Specification recites that Applicants discovered, using an acetic acid writhing test, that a "weight ratio of 1:5 of oxycodone and dextromethorphan provides optimal efficacy." Page 5 at Lines 21-22. The Specification further reads, in pertinent part, that:

> Applicants have further found that use of lesser amounts of dextromethorphan, i.e. use of weight ratios lower than 1:5, does not maximally potentiate the oxycodone. On the other hand, use of greater amounts of dextromethorphan, i.e. use of weight ratios greater than 1:5, does not provide analgesic efficacy in excess of the 1:5 weight ratio.

Page 6 at Lines 5-8.

Guittard et al. teach a "therapeutic composition and the compositional bilayer to be surrounded by a wall comprising a semipermeable composition with an exit for delivering the therapeutic composition to a human patient in need of oxybutynin therapy." Col. 5 at Lines 32-36.

CHANDLER & UDALL, LLP
4801 E. BROADWAY BLVD
Tucson, Arizona 85711

TEL 520-741-7636
FAX 520-746-9114

Guittard et al. teach away from Applicants' claim 1, as amended herein. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994); *see KSR*, 127 S. Ct. at 1739-40 (explaining that when the prior art teaches away from a combination, that combination is more likely to be nonobvious).

Guittard et al. teach forming an encapsulated bilayer table to include an exit extending through the encapsulant but not into the oxybutynin layer, i.e. not into the actives layer. For example, Guittard et al. teach "in one manufacture the beneficial drug oxybutynin and other ingredients comprising a therapeutic composition or **comprising the first layer facing the exit means** are blended, or they are blended then pressed into a solid layer." Col. 6 at Line 67 through Col, 7 at Line 4. Similarly, "[a] passage way is laser drilled or mechanically **drilled through the wall to contact the oxybutynin layer** . . ." Col. 6 at Lines 17-19. Once again, "the semipermeable walled, bilayered tablet was laser drilled **to provide a 20 mil (0.51 mm) orifice to contact the oxybutynin layer** and the exterior of the dosage form." Col. 11 at Lines 9-11.

A person of ordinary skill in the art following the teachings of Guittard et al. would find motivation to form an oral dosage form to include an aperture extending through an encapsulating layer to contact a tablet comprising a therapeutic composition. One of ordinary skill in the art would not, however, find motivation to form an oral dosage form to include an aperture extending through an encapsulating layer and further extending into a tablet comprising a therapeutic composition, as recited in claim 1, as amended herein.

CHANDLER & UDALL, LLP
4801 E. BROADWAY BLVD
Tucson, Arizona 85711

TEL 520-741-7636
FAX 520-746-9114

In *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 167 L. Ed. 2d 705 (2007), the Supreme Court held that the obviousness analysis of *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 86 S. Ct. 684, 15 L. Ed. 2d 545 (1966), controls an obviousness inquiry. The *Graham* obviousness factors include "the scope and content of the prior art" and the "differences between the prior art and the claims". *KSR*, 127 S. Ct. at 1734 (quoting *Graham*, 383 U.S. at 17-18).

Neither Mayer et al. nor Guittard et al., singly or in combination, teach or suggest an oral dosage comprising a first layer comprising oxycodone hydrochloride and dextromethorphan hydrobromide, wherein the weight ratio between the oxycodone hydrochloride and the dextromethorphan hydrobromide is 1:5, in combination with a second layer comprising carboxy methyl cellulose, as recited by Applicants' claim 1, as amended herein. In addition, neither Mayer et al. nor Guittard et al., singly or in combination, teach or suggest an oral dosage comprising a bilayer tablet comprising an actives layer comprising oxycodone/dextromethorphan layer, and an encapsulant, wherein the oral dosage is formed to include an aperture extending through the encapsulant and further extending into the actives layer, as recited by claim 1, as amended herein.

Thus, the prior art differs from the elements of Applicant's claim 1, as amended. To further illustrate the significant differences between the prior art and claim 1, Applicant directs the Examiners attention to the Declaration of George R. Krsek (hereinafter "Krsek"). The inventor herein, namely George R. Krsek, compared the release profiles of a first oral dosage form with a second oral dosage form, wherein both dosage forms comprised a bi-layer tablet comprising 210 milligrams of active ingredients in an active layer, an osmagen layer, and an

CHANDLER & UDALL, LLP
4801 E. BROADWAY BLVD
Tucson, Arizona 85711

TEL 520-741-7636
FAX 520-746-9114

encapsulant, wherein in the first oral dosage form an aperture extended through the encapsulant but did not extend into the active layer, and wherein in the second oral dosage form an aperture extended through the encapsulant and further extended into the active layer. Krsek Declaration ("Krsek") at Paragraphs 10 - 32. Thus, the first Krsek oral dosage form follows the teachings of Guittard et al., but the second Krsek dosage form reads on claim 1, as amended herein.

Referring once again to Guittard et al., FIG. 1 depicts the cumulative amount of dose released over time. Col. 15 at Lines 22-25. Using the oral dosage form taught by Guittard et al., all of the active dosage is not released until about 24 hours. Guittard et al. at FIG. 1.

Exhibit 2 to the Krsek Declaration graphically shows the cumulative release of active ingredients over time for both the first Krsek oral dosage form and the second Krsek oral dosage form. Krsek at Paragraphs 16 and 23. Exhibit "B" further graphically shows the Inventor's Ideal Release Profile. Krsek at Paragraph 11.

The release profile for the first Krsek oral dosage form, which follows the teachings of Guittard et al., shows that all the active ingredients are not released until about 24 hours. Thus, the release profile for the first Krsek dosage parallels the release profile shown in Guittard et al. FIG. 1.

In marked contrast, the release profile for the second Krsek oral dosage form, which reads on claim 1, as amended herein, shows that the active ingredients are released within 4 hours. Krsek at Paragraph 25. Moreover, the release profile for the second Krsek oral dosage form more closely approximates the inventor's Ideal Release Profile than does the first Krsek oral dosage form.

Exhibit "C" to Krsek graphically shows the cumulative amounts of Actives released

CHANDLER & UDALL, LLP
4801 E. BROADWAY BLVD
Tucson, Arizona 85711

TEL 520-741-7636
FAX 520-746-9114

over the first 4 hours from the first oral dosage form and the second oral dosage form. Krsek at Paragraph 26. After about 1 hour, the two oral dosage forms released about the same amount of Actives. Krsek at Paragraph 27. After about 2 hours, the second oral dosage form released about 1.7 times the amount of Actives as the first oral dosage form. Krsek at Paragraph 28. In light of the comparable amounts of Actives released by the two dosage forms after about 1 hour, the increased amount released by the second oral dosage form after about 2 hours was unexpected. Krsek at Paragraph 29. After about 4 hours, the second oral dosage form released about 2.6 times the amount of Actives as the first oral dosage form. Krsek at Paragraph 30. In light of the comparable amounts of Actives released by the two dosage forms after about 1 hour, the increased amount released by the second oral dosage form after about 4 hours was unexpected. Krsek at Paragraph 31.

In summary, the Guittard et al. oral dosage form and the first Krsek oral dosage form are useful where a continuous, sustained drug release over about 24 hours is desired. In contrast, the second Krsek oral dosage which reads on claim 1, as amended herein, is useful where a rapid initial release to a threshold concentration over a short period of time is desired, with little incremental release thereafter.

In light of the scope and content of the prior art, and in light of the differences between that prior art and claim 1, as amended herein, Applicant respectfully submits that claim 1, as amended is patentable over the combined teachings of Mayer et al. and Guittard et al.

Claims 2-6, as amended herein, depend, directly or indirectly, from claim 1, as amended herein. Under 35 U.S.C. § 112, fourth paragraph, "a claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers." "If an

CHANDLER & UDALL, LLP
4801 E. BROADWAY BLVD
Tucson, Arizona 85711

TEL 520-741-7636
FAX 520-746-9114

independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious." MPEP 2143.03; *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed.Cir. 1988). Applicants respectfully submit that claims 2-6, as amended herein, are patentable over the combined teachings of Mayer et al. and Guittard et al..

Having dealt with all of the outstanding objections and/or rejections of the claims, Applicants submit that the application as amended is in condition for allowance, and an allowance at an early date is respectfully solicited. In the event there are any fee deficiencies or additional fees are payable, please charge them, or credit an overpayment, to our Deposit Account No. 502262.

Respectfully submitted,

/Dale F. Regelman/

Dale F. Regelman, Ph.D.
Attorney for Applicants
Reg. No. 45,625

CERTIFICATE OF ELECTRONIC FILING

I hereby certify that this correspondence is herewith being electronically transmitted via Electronic Filing System to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

/Reena Mendez/
Signature

November 14, 2007
Date of Signature

CHANDLER & UDALL, LLP
4801 E. BROADWAY BLVD
Tucson, Arizona 85711

TEL 520-741-7636
FAX 520-746-9114